Long-term follow-up reduces type 2 diabetes risk

Type 2 diabetes is an inherited disease, but habits can affect the risk of getting it. Obesity due to fatty and high-calorie foods, often in combination with limited activity, increases the risk considerably. A new study at NTNU and St. Olav's Hospital Centre of Obesity has followed people in the risk group for five years. Participants were offered organized physical activity and courses on diet.

"We're seeing that follow-up from the health services in Norwegian municipalities over a long period of time can help reduce the risk of developing diabetes 2 and improve people's health," says Ingrid Sørdal Følling, a researcher at NTNU's Department of Health and Nursing.

Worldwide, 350 million people have type 2 diabetes. Affected individuals either do not produce enough insulin, or their cells resist the hormone, called insulin resistance. This affects blood sugar levels and disrupts the metabolism of nutrients such as carbohydrates, fats and proteins in the body.

However, it often helps to take action, the new research shows. Changes in habits can be beneficial – if you actually implement them. That's where long-term follow-up is needed.

The study involved 189 people with a BMI of 25 or higher. Nine people already had symptoms of type 2 diabetes when they started, and six of them reduced their symptoms.

Other research has shown that simple lifestyle advice from people in the health care system does not reduce the risk of developing type 2 diabetes. However, the participants in this study were offered physical activity and dietary courses for one year, and were followed up with measurements over a long period, in the case of this study for a full five years. Having a long-term commitment appears to yield much better results.

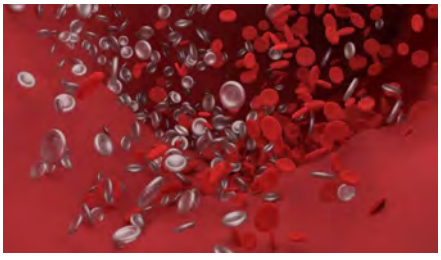
Fifty-four of the participants dropped out during the five years of the study, corresponding to just over 30 per cent. Many of the youngest participants and those with the highest BMI, waist circumference and weight measurement were among the dropouts.

The researchers do not know exactly why these individuals chose not to carry on. There may be socio-economic reasons, since the people who did not participate for the length of the project had less education and fewer were employed. Another possible explanation is that the training and courses were scheduled during the day, which might have made it more difficult for younger people to participate.

Blood type may predict which cancer patients are more likely to develop blood clots

Cancer patients' blood type may play a role in their risk for dangerous blood clots, researchers say.

Cancer and its treatments increase the risk for venous thromboembolism (VTE). That includes deep-vein thrombosis (DVT, a blood clot that typically forms in the deep veins of the leg) and pulmonary embolism (PE, a life-threatening condition that occurs when a blood clot breaks free and travels to the lungs' arteries).



Factors such as tumor or cancer type are now used to identify cancer patients at high risk of VTE, but many go unidentified. This study concluded that cancer patients with non-O blood types, such as types A, B and AB, are at increased risk for VTE.

"We've known tumor type helps determine the baseline risk for VTE," said study author Cornelia Englisch, a doctoral student at the Medical University of Vienna. "But we continue to see that these risk assessments fail to capture all cancer

patients who develop these blood clots. By solely assessing tumor type, we miss up to 50% of people who develop VTE."

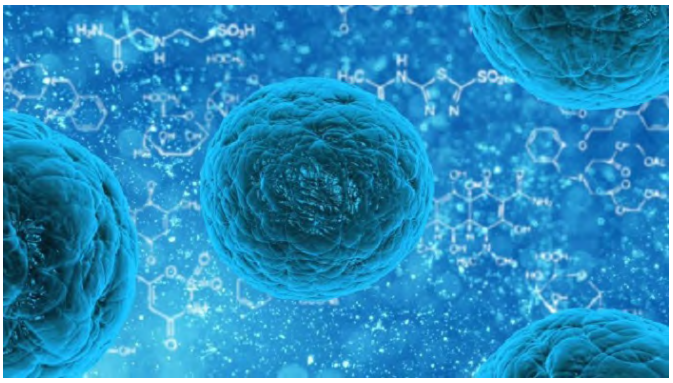
The findings from an analysis of data from more than 1,700 people in Austria with a new or recurrent cancer diagnosis were published in the journal Blood Advances. The researchers reported that cancer patients with non-O blood types were more likely to develop VTE three months after their diagnosis or cancer recurrence.

Englisch said the increased risk is not apparent at the time of diagnosis, because cancer therapies increase the odds of developing blood clots. The investigators also found that patients with non-O blood types and tumors outside the high-risk disease category were more likely to develop clots. This shows that relying solely on tumor type to assess VTE risk may miss many at-risk patients.

Further research is needed before blood typing might prove useful in assessing cancer patients' VTE risk. "Blood typing is easy to perform, can be done worldwide, and doesn't require any specialized background knowledge or equipment," Englisch said in a news release by Blood Advances. "And of course, every risk factor that we identify helps us to understand these life-threatening complications in cancer patients better," she added. "Perhaps this will create awareness for the role blood types can play as clinical biomarkers."

First roadmap that traces the development of human blood stem cells

UCLA scientists and colleagues have created a first-of-its-kind roadmap that traces each step in the development of blood stem cells in the human embryo, providing scientists with a blueprint for producing fully functional blood stem cells in the lab.



The research, published recently in the journal *Nature,* could help expand treatment options for blood cancers like leukemia and inherited blood disorders such as sickle cell disease, said Dr. Hanna Mikkola who led the study.

For decades, doctors have used blood stem cells from the bone marrow of donors and the umbilical cords of newborns in life-saving transplant treatments for blood and immune diseases. However, these treatments are limited by a shortage of matched donors and hampered by the low number of stem cells in cord blood.

Researchers have previously attempted to create blood stem cells in the lab from human pluripotent stem cells, which can potentially give rise to any cell type in the body. But success has been elusive, in part because scientists have lacked the instructions to make lab-grown cells differentiate into self-renewing blood stem cells rather than short-lived blood progenitor cells, which can only produce limited blood cell types.

"We now have a manual of how hematopoietic stem cells are made in the embryo and how they acquire the unique properties that make them useful for patients," said UCLA scientist Vincenzo Calvanese in a news release.

The research team, which included scientists from Germany and Australia created the resource using single-cell RNA sequencing and spatial transcriptomics, new technologies that enable scientists to identify the unique genetic networks and functions of thousands of individual cells and to reveal the location of these cells in the embryo.

The data make it possible to follow blood stem cells as they emerge from the hemogenic endothelium and migrate through various locations during their development, starting from the aorta and ultimately arriving in the bone marrow. Importantly, the map unveils specific milestones in their maturation process, including their arrival in the liver, where they acquire the special abilities of blood stem cells.

The research group also pinpointed the exact precursor in the blood vessel wall that gives rise to blood stem cells. This discovery clarifies a longstanding controversy about the stem cells' cellular origin and the environment that is needed to make a blood stem cell rather than a blood progenitor cell.

Now that the researchers have identified specific molecular signatures associated with the different phases of human blood stem cell development, scien-

tists can use this resource to see how close they are to making a transplantable blood stem cell in the lab.

In addition, the map can help scientists understand how blood-forming cells that develop in the embryo contribute to human disease. For example, it provides the foundation for studying why some blood cancers that begin in utero are more aggressive than those that occur after birth.

Insomnia linked with recurrent heart events in coronary patients

Nearly half of heart disease patients have insomnia, according to research presented at ESC Preventive Cardiology 2022, a scientific congress of the European Society of Cardiology (ESC), and published in SLEEP Advances.

"Sleep problems are linked to mental health issues, but our study found that insomnia was still significantly associated with heart events even after accounting for symptoms of anxiety and depression," said lead author Lars Frojd, a medical student at the University of Oslo, Norway. "The findings suggest that heart patients should be assessed for insomnia and offered appropriate management."

The prospective study included 1,068 consecutive patients an average age of 16 months after a heart attack and/or a procedure to open blocked arteries (stent implantation or bypass surgery). Data on insomnia, risk factors for repeat heart events, and co-existing conditions were collected at baseline.

Participants completed the Bergen Insomnia Scale questionnaire which is based on the diagnostic criteria for insomnia. Six questions cover the ability to fall asleep and stay asleep, waking up prematurely, feeling inadequately rested, tiredness during the day that affects ability to function at

work or socially, and being dissatisfied with sleep.

The risk factors included C-reactive protein (a marker of inflammation), smoking status, low-density lipoprotein (LDL) cholesterol, diabetes, physical activity, waist circumference, and systolic blood pressure. The co-existing conditions were stroke, transient ischaemic attack, peripheral artery disease, and kidney failure.

Patients were followed for the primary composite endpoint of major adverse cardiovascular events (MACE), defined as cardiovascular death, hospitalisation due to myocardial infarction, revascularisation, stroke or heart failure. Outcome data were obtained from hospital records.

Approximately one in five participants (21%) were women. At baseline, the average age of patients was 62 years, almost half (45%) had insomnia and 24% had used sleep medication in the past week. During an average follow-up of 4.2 years, a total of 364 MACE occurred in 225 patients.

Compared to those without insomnia, the relative risk of recurrent MACE in patients with insomnia was 1.62 after adjusting for age and sex, 1.49 after additional adjustment for coronary risk factors, and 1.48 after also adjusting for co-existing conditions. The association between insomnia and recurrent MACE remained significant when symptoms of anxiety and depression were also adjusted for, with a relative risk of 1.41.

Insomnia accounted for 16% of recurrent MACE in attributable risk fraction analyses, being third in importance after smoking (27%) and low physical activity (21%). Mr. Frojd said: "This means that 16% of recurrent major adverse cardiovascular events might have been avoided if none of the participants had insomnia."

He concluded: "Our study indicates that insomnia is common in heart disease patients and is linked with subsequent cardiovascular problems regardless of risk factors, co-existing health conditions and symptoms of mental health. Further research is needed to examine whether insomnia treatments such as cognitive behavioural therapy and digital applications are effective in this patient group."

A bandage that could accelerate healing of diabetic ulcers developed

A scientific team of scientists from National University of Science and Technology (NUST) MISIS and Institute of Cytology and Genetics of SB RAS managed to create innovative bandages based on organic polymers and silver nanoparticles, which stimulate the healing of diabetic ulcers and chronic wounds. The results of the work have been published in Pharmaceutics.

Type 2 diabetes mellitus causes the body to becomes especially vulnerable to infections. In addition, diabe-

tes affects blood circulation, hindering the delivery of nutrients. This leads to slow wound healing, and also increases the likelihood of developing complications in the form of bacterial infection.

To ensure successful healing, excessive exudate (liquid released into the tissue in case of damage) must be delayed, providing good oxygenation, a moist environment, and sterility. To solve this complex problem, a team of materials scientists from NUST MISIS used substances from the class of polysaccharides — organic polymers that can absorb and retain aqueous solutions hundreds of times their own dry weight.

"We took two substances as a basis. Chitosan is a well-known carbohydrate polymer derived from the chitinous cover of crustaceans, which has many potential clinical applications due to its antibacterial, anticoagulant, anti-tumor and hemostatic properties. Kurdlan is a homopolysaccharide from the category of β-glucans and shows a positive effect on the human immune system, providing antitumoral and antimicrobial effects," said the author of the study, a researcher at the NUST MISIS Inorganic Nanomaterials Laboratory Elizaveta Permyakova in a news release.

The developers have synthesized a therapeutic agent in the form of foam based on chitosan and curdlan. It has been obtained by lyophilization — soft drying of the dissolved mixture, when the drug to be dried is frozen and then placed in a vacuum chamber where the solvent is removed.

"To enhance the antibacterial properties and stimulate the immune system, during the polymerization process, we have added a solution of silver nitrate to the mixture of curdlan/chitosan, which was subsequently reduced to silver nanoparticles under the influence of UV irradiation. In vivo tests in mice with genetically determined type 2 diabetes revealed an enhanced effect of silver modified foam: it significantly accelerates the regeneration process compared to pure foam and the untreated control," added Elizaveta Permyakova.

According to the authors, the resulting foamy substance has antibacterial and super-absorbent properties that allow localization of exudate in the form of a soft gel, provides good oxygenation of the wound surface and prevents bacterial infection. In addition, the silver nanoparticles in the composition stimulate the immune system, which accelerates the healing process.

The team is currently completing testing of the resulting material as part of *in vivo* preclinical studies.

A new strategy to treat diabetes may be on the cards that does not involve taking drugs

Scientists claim to have discovered a strategy to treat diabetes that does not require the use of insulin. The therapy appears to have succeeded in animals, and human trials are next on the agenda. Yale School of Medicine (YSM) researchers have demonstrated the ability to use ultrasound to stimulate specific neurometabolic pathways in the body to prevent or reverse the onset of type 2 diabetes in three different preclinical models.

The study, published in Nature Biomedical Engineering, represents a significant milestone in the field of bioelectronic medicine, which is exploring new ways to treat chronic diseases such as diabetes using novel medical devices to modulate the body's nervous system.

Type 2 diabetes affects millions of people worldwide. Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.

The team of investigators, led by Raimund Herzog tested the magnitude of the effect of ultrasound treatment on blood glucose. "Even though we already have a large variety of anti-diabetic medications available to us to treat high glucose levels, we are always looking for new ways to improve insulin sensitivity in diabetes," Herzog said.

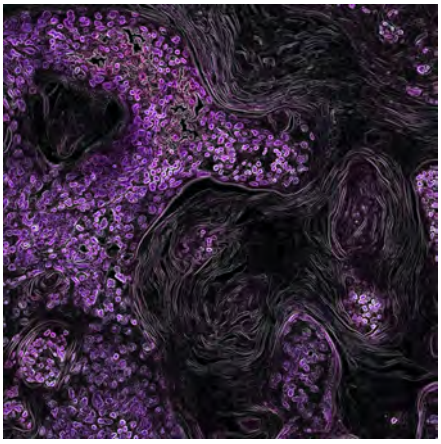
"Unfortunately, there are currently only very few drugs that lower insulin levels," Herzog further said in a news release. "If our ongoing clinical trials confirm the promise of the preclinical studies reported in this paper, and ultrasound can be used to lower both insulin and glucose levels, ultra-

sound neuromodulation would represent an exciting and entirely new addition to the current treatment options for our patients."

Following the reported preclinical studies, the collaborators have been engaged in additional studies that investigate the effects of alternate dosing such as the type of ultrasound pulse and duration of treatment. The team is expected to report on those studies later this year.

The goal of the studies is to provide long-lasting treatment for people with type 2 diabetes to alleviate and potentially reverse the disease.

Lung cancer drug could improve survival rates for bladder cancer patients undergoing chemotherapy



Scientists from the University of Sheffield have discovered a drug already used to treat lung cancer could help to improve survival rates for bladder cancer patients. Researchers found that adding nintedanib - a targeted cancer growth inhibitor currently used to treat non-small cell lung cancer - to chemotherapy, could significantly improve overall survival rate for bladder cancer patients at one, two and five years.

A total of 120 patients from 15 hospitals in the UK were recruited for the NEOBLADE phase two randomised control trial, led by Professor Syed A Hussain from the University of Sheffield's Department of Oncology and Metabolism.

The primary outcome of the study was to establish if adding the drug nintedanib - which blocks different proteins from sending signals to cancer cells to grow - could improve the pathological complete response (the absence of all detectable cancer after treatment) of patients undergoing chemotherapy for muscle-invasive bladder cancer.

Although the study, published in *The Lancet Oncology*, did not find significant improvement for this primary outcome, results showed adding nintedanib did improve overall survival rate - something which now requires further investigation in larger trials.

Professor Syed A Hussain, Professor of Medical Oncology at the University of Sheffield, said: "This is a very exciting and important trial. Although we did not see an improvement in adding nintedanib to chemotherapy in terms of immediate outcome of pathological complete response, we found promising results in terms of improving the overall survival rate of bladder cancer patients.

"These results could be related to changes in the microenvironment of cancer cells translating into survival benefit." "The study also showed that the treatment - which patients can take at home in tablet form - was well tolerated. This is extremely positive as it does not appear to add significant side effects to those already experienced by patients undergoing chemotherapy."

Professor Hussain added, "We are particularly eager to explore the potential impact of adding this targeted cancer drug to the standard care of chemotherapy on those patients with alteration in specific biomarkers targeted by this drug who may be at much higher risk of cancer cells leaving the tumour and spreading throughout the body."

Administering lithium may slow down kidney aging

Best known therapeutically as a treatment for bipolar disorder, lithium has long intrigued researchers with its potential age-defying properties. The element has been shown in lab experiments to extend the lifespan of fruit flies and roundworms, while observational studies have suggested tap water naturally laced with trace amounts of lithium might improve human longevity.

Researchers at The University of Toledo have recently found that low-dose lithium acts as a powerful anti-aging agent in the kidneys.

Dr. Rujun Gong, UToledo professor of medicine, said, "As people are living longer than ever, it's crucial we find ways to slow or halt kidney aging. Our findings suggest

lithium may indeed have significant potential to do just that, reducing the burden of renal disease."

Kidney function tends to decline as people age, by as much as 50%, even in the absence of any identifiable kidney disease. This can be an important health issue for many elderly patients, increasing their risk of developing kidney failure and complicating treatment of many other medical conditions.

Gong's research was recently published in the *Journal of Clinical Investigation.*

While lithium is a highly effective mood stabilizer and first-line treatment for bipolar disorder, scientists still don't know exactly how it works in the brain. However, researchers have found that one of the major molecular targets of lithium is GSK3-beta — an enzyme that is associated with cellular aging in the kidney and a decline in kidney function.

In close collaboration with Dr. Lance Dworkin, professor and chair of the Department of Medicine and a nephrologist at UToledo, Gong and his colleagues first demonstrated that knocking out the gene responsible for producing GSK3-beta slowed kidney aging and preserved kidney function in animal models. Researchers then used lithium chloride to inhibit GSK3-beta, which achieved similar results. Mice had lower levels of albuminuria, or protein in the urine, improved kidney function and less cellular deficiency compared to a control group.

"We wanted to directly target GSK3-beta. There are a lot of fancy, very expensive small molecule compounds being developed, but we recognized that lithium has been used as a standard inhibitor of GSK3-beta in basic science research for decades and it's a safe and widely used FDA-approved drug," Dworkin said. "Our results very clearly showed low-dose lithium attenuates kidney aging in mice."

To further validate their findings, researchers also reviewed a group of psychiatric patients to assess their kidney health. Laboratory tests showed individuals who had received long-term treatment with lithium carbonate had better functioning kidneys than those who had not received lithium treatments, despite comparable age and comorbidities.

"One of the pitfalls of lithium as a psychiatric medication is that the therapeutic window is very narrow. Because of the blood-brain barrier, the effective psychiatric dose for lithium is very close to the toxic dose," Gong said. "But you only need a really small dose to produce the anti-aging effect in other organs."

A protein associated with detection of cold and menthol may also cause migraines

Scientists have provided the strongest evidence yet that a protein that enables us to detect the sensation of cold may also be responsible for migraines. The findings appear in the journal PAIN.

About 10% of all humans suffer from migraine — nearly 800 million people globally.

Scientists at the USC Dornsife College of Letters, Arts and Sciences have found that blocking or removing a protein called TRPM8 in mice prevented them from experiencing migraine-like symptoms. In previous work, the researchers determined that TRPM8, found in nerve cells, is important for sensing cold, including the cool sensation of menthol.

The study reinforces previous genomics studies that hinted at TRPM8's involvement in migraine.

"Our results confirm the importance of TRPM8 in migraines that was suggested by human genome-wide association studies and implicate the protein as a potentially important component of the pathology that leads to migraine. Thus, other scientists or clinicians can now add TRPM8 to their models of migraine and potential targets for treatment."—says David McKemy, professor of biological sciences at USC Dornsife and corresponding author on the study in a news release.

McKemy and his team studied mice that were genetically engineered to lack TRPM8. They gave the mice either nitroglycerin or a peptide known as CGRP, both of which can induce migraine-like symptoms including spontaneous pain and evoked pain.

"We showed that both spontaneous pain and

evoked pain that is induced in mice by treatments with nitroglycerin and CGRP was absent in mice genetically modified to not make the TRPM8 protein or lack the nerves that normally contain TRPM8," McKemy said. "The results show that TRPM8 is necessary for migraine-like pain in mice."

"We showed that we could treat mice with a drug that blocks TRPM8 function and prevent migraine-like pain," he said, giving further evidence that TRPM8 is a strong candidate target for new anti-migraine drugs.

The researchers now aim to answer new questions arising from their work, including How does TRPM8 mediate migraine-like pain at the molecular and cellular level? Are migraineurs predisposed to headaches due to mutations in TRPM8 or is it something in the cellular processes that alter TRPM8 function? Can blocking TRPM8 function in humans with medicines be a method of treatment?

Could unsaturated fats aggravate diabetes? Study sheds light

Scientists at Nanyang Technological University, Singapore's (NTU Singapore) Lee Kong Chian School of Medicine (LKC Medicine) have mapped a novel cellular pathway that shows that saturated fat contributes to the development of diabetes and can worsen the disease, underscoring its role in metabolic diseases.

Through experiments on laboratory-cultured mouse cells and on mice fed with a diet rich in saturated fat, the NTU Singapore scientists found that saturated fatty acids can degrade a protein called FIT2, triggering a chain of molecular events that cause insulin-producing cells to lose their function and die.

When these cells die, the body's ability to secrete enough insulin in response to carbohydrates is impaired, resulting in diabetes. Partially restoring FIT2 levels in insulin-producing cells, however, could mitigate the damage caused

by saturated fat, the scientists found.

These findings, reported in the scientific journal Proceedings of the *National Academy of Sciences (PNAS)*, point to the potential of increasing FIT2 production in the body as a new method to manage diet-induced diabetes. Also called Type-2 diabetes, the metabolic condition accounts for 95 percent of diabetes cases, affecting about 462 million people globally.

The scientists said that the study also reinforces, for diabetic patients, the importance of moderating their meat and dairy consumption, in addition to sugar and carbohydrates, since saturated fat is found in high amounts in red meats, processed meats, and dairy products.

Associate Professor Yusuf Ali, Program Director of Nutrition, Metabolism & Health at NTU LKCMedicine and lead author of the study, said in a news release. "Studies have identified saturated fat as the 'unhealthy fat' that leads to diabetes, but the mechanisms have been unclear. Our study confirms this link and maps out a pathway through which this happens. We also identify a new protein that we could target with new therapies to help manage the illness. In terms of nutrition, the findings suggest that diabetic patients who turn to proteins in place of white rice may need to watch their intake of saturated fats, which are found in high levels in red meats and other meat and dairy products.

How Genetic fingerprints could aid doctors diagnose and manage skin conditions effectively

For decades, clinicians have largely been diagnosing rashes by eye. While examining the physical appearance of a skin sample under a microscope may work for more obvious skin conditions, many rashes can be difficult to distinguish from one another.

At the molecular level, however, the differences between rashes become clearer. Scientists have long known that molecular abnormalities in skin cells cause the redness and scaliness seen in conditions like psoriasis and eczema. While almost all the various cell types

in your skin can release chemicals that worsen inflammation, which ones leads to rash formation remains a mystery and may vary from patient to patient.

Using a new approach, Raymond J. Cho along with colleagues analyzed the genetic profiles of skin rashes and quantitatively diagnosed their root causes.

High-res skin profiles

Traditional genetic analyses work by averaging out the activity of thousands of genes across millions of cells, writes Cho in an article, originally published in The Conversation.

Clinicians collect and analyze tumor biopsies from patients to determine a particular cancer's unique molecular characteristics. Cancer cells lend themselves to this form of testing because they often grow into recognizable masses that make them easy to isolate and analyze. But skin is a complex mixture of cells. Collapsing these unique cell communities into a single group may obscure genetic signatures essential to diagnosis.

Instead of averaging the genetic signatures across all cell types in bulk, single-cell RNA sequencing analyses allow each cell to preserve its unique characteristics. Using this approach, Cho along with his colleagues isolated over 158,000 immune cells from the skin samples of 31 patients and measured the activity of about 1,000 genes from each of those cells to create detailed molecular fingerprints for each patient.

"By analyzing these fingerprints, were able to pinpoint the genetic abnormalities unique to the immune cells residing in each rash type. This allowed us to quantitatively diagnose otherwise visually ambiguous rashes," Cho stated.

"We also observed that some patients had treatment responses consistent with what we expected with our predicted diagnoses. This suggests that our concept could viably be expanded for further testing," Cho added.

A database of genetic finger prints

"To make our approach available to clinicians and scientists, we developed an open-source web database called RashX that contains the genetic fingerprints of different rashes. This database will allow clinicians to compare the genetic profile of their patients' rashes to similar profiles in our database. A closely matching genetic fingerprint might yield clues as to what caused their patient's rash and lead to potential treatment avenues."

Furthermore, chronic inflammatory diseases that affect organs other than the skin share similar genetic abnormalities. Lab tests that can illuminate the root causes of skin diseases can likely be expanded to many other conditions.

Atlas of migraine cell types sheds light on new therapeutic targets

Headaches such as migraine are among the leading causes of morbidity worldwide, but most treatments provide only partial relief. While scientists know that migraine and related headaches are caused by activity in a part of the nervous system known as the trigeminal ganglion (TG), it remains unclear which genes and cell types of the TG are involved. By analyzing both human and mouse TG, investigators from Brigham and Women's Hospital and Massachusetts General Hospital profiled, at single-cell resolution, the genes expressed in each TG cell type. Their research, published in Neuron, will allow researchers to design more effective treatments for pain by selectively targeting certain genes and cells.

"Very few pain therapeutics have made it to the clinic, despite strong efficacy in animal models, so our goal was to analyze human tissue to look for new targets for headache and facial pain treatment," said William Renthal, from the Department of Neurology at Brigham said in a news release. "We now have an atlas of the genes that are expressed in each of the cell types in the TG — the key relay center for migraine and facial pain — and we are now using this tool to identify potential therapeutic targets that are selectively expressed in cell types that drive head pain. We believe this will lead to more precise medicines without as many side effects."

In addition to analyzing the TG of four human donors, the researchers studied two mouse models of headache. Importantly, they found that while cell types between mice and humans are largely conserved, some of the genes known to be involved in pain are expressed in different subsets of cells in mice versus humans. This gave the researchers new ideas about which cells to study further.

"A major value of this study is that it wasn't limited to one spe-

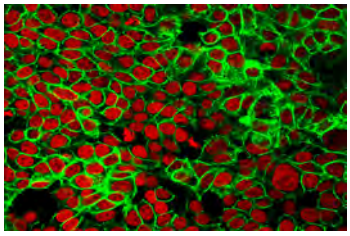
cific cell-type or branch of the trigeminal ganglion," said Jochen K. Lennerz of the Center for Integrated Diagnostics in the Department of Pathology at MGH. Lennerz's lab performed the complex tissue-harvesting procedures required to extract the TG, which is located inside the cranium but has neurons that enervate the teeth, eyes, and other facial structures. "We included all of the cells that make up the TG," he said.

The information from the researchers' atlas, which is available publicly online, could prompt new investigations into the molecular basis of different varieties of pain, such as tooth pain. It may also shed light on how to treat head pain beyond migraine, including post-concussive headaches or cluster headaches.

Going forward, the researchers plan to improve the current atlas by sequencing additional human tissues. They hope that the atlas can help researchers develop more selective pain therapeutics by targeting, through gene therapies, the specific cells they've identified.

New method developed for detecting tumor cells with specificity and selectivity

The Center for Nuclear Receptors and Cell Signaling at the University of Houston has developed a new way to detect very rare and highly heterogeneous circulating tumor cells with high specificity and sensitivity. The UniPro device is reported in the journal Molecular *Therapy*.



Circulating tumor cells (CTC), which are detached from primary tumors to enter the bloodstream, are particularly hard to detect. Only a few of these rare malignant cells are typically found among millions of white blood cells and billions of red blood cells per milliliter of blood.

"CTCs, like the tumors they are originally detached from, lack unique and well-defined universal biomarkers highlighting the challenges of detection specificity," reports Dr. Shaun Zhang, Anderson Professor of biology and biochemistry. "We report a novel method that is based on a chimeric virus probe and can detect CTCs with extremely high specificity and sensitivity. Moreover, it exclusively detects live CTCs, and its detection efficacy is not impacted by the variation of epithelial cell adhesion molecule expression."

Chimeric properties combine two viruses together. The outside of the UniPro chimeric virus probe is coated with the human papillomavirus to test blood samples. The probe provides high specificity as it is sent only inside the CTC and not to other blood cells. The primary importance of CTCs is their ability to seed metastatic tumors, their constant presence in the blood have made their detection an attractive alternative to the traditional biopsy for clinical applications such as cancer screening, therapy evaluation and disease prognosis.

Current methods of detecting CTCs mainly rely on immunological detection of protein markers on the tumor cells. They suffer from two main drawbacks. First, when tumor cells get into the blood, they intend to undergo a biological change called epithelial-mesenchymal transition (EMT). CTCs usually lose the protein markers after EMT, hence won't be detectable by the current method. Second, the current method detects both nonviable and viable CTCs.

Unambiguously detecting live circulating tumor cells opens the door for many clinical applications, such as convenient and instantaneous monitoring of the effectiveness of clinical cancer treatment and monitoring cancer relapse.

Team discovers novel root cause of tau-induced neurodegeneration

Researchers from The University of Texas Health Science Center at San Antonio (UT Health San Antonio) reported the discovery of a novel mechanism by which pathological forms of tau protein cause neurons to die. Alzheimer's disease and chronic traumatic encephalopathy (CTE) are among more than 20 disorders that include tau protein pathology.

The newly found mechanism of tau-induced damage can be altered pharmacologically, the scientists noted, making it a novel target for drug development. The study, published in *Alzheimer's & Dementia:* The Journal of the *Alzheimer's* Association, provides a framework for future studies in vertebrate models of tauopathy and eventually clinical trials in people.

"Nonsense-mediated mRNA decay is a key step in the process by which genetic information is translated into proteins," Zuniga said. Impairment of this quality-control

mechanism results in buildups of RNA and production of abnormal, dysfunctional proteins. "It has an absolutely detrimental effect," Zuniga said.

DNA contains the genetic blueprints for proteins. Messenger RNA reads out the blueprints to make proteins. This information highway becomes logjammed when nonsense-mediated mRNA decay is reduced.

Treatments for Alzheimer's disease and other tauopathies have failed in part because they focused on clearing tau protein or another protein called amyloid beta. Amyloid beta plaques and tau tangles are classic hallmarks of Alzheimer's.

Identifying multiple mechanisms underlying tau pathology could result in understanding which patients might benefit from which therapies, said Nicolas Musi, MD, professor of medicine at UT Health San Antonio and director of the Sam and Ann Barshop Institute. A subset of Alzheimer's disease patients might be responsive to a drug that increases nonsense-mediated mRNA decay, for example.

Threat of untreatable gonorrhoea could be tackled using an existing meningitis vaccine

Gonorrhoea is a sexually transmitted infection (STI) which, if untreated, can lead to serious health conditions, including infertility in women, transmission to newborn babies, and increased risk of HIV. Declining effectiveness of drug treatments for the bacteria responsible – *Neisseria gonorrhoeae* – and the lack of a licensed vaccine to prevent the infection have raised concerns about the possibility that gonorrhoea may become more resistant to treatment, or even untreatable, in future.

Meningitis vaccines have been recommended by the WHO as part of its roadmap to reduce the global burden of meningitis. This includes offering meningitis vaccines as part of routine childhood immunisation strategies. Since meningitis vaccines have become more widely available, studies have shown they also offer some protection against gonorrhoea, and that even partial protection could reduce cases of the infection considerably.

An observational study led by Dr Winston Abara, of U.S. Centers for Disease Control and Prevention, used health records to identify laboratory-confirmed cases of gonorrhoea and chlamydia – another leading STI – among 16–23-year-olds in New York city, revealed that there were more than 167,000 infections (18,099 gonorrhoea, 124,876 chlamydia, and 24,731 co-infections) among almost 110,000 people. A total of 7,692 people had received the 4CMenB vaccine, with 4,032 (52%) receiving one dose, 3,596 (47%) two doses, and 64 (less than 1%) more than two doses. Full 4CMenB vaccination – receiving two doses – was estimated to provide 40% protection against gonorrhoea. One vaccine dose provided 26% protection.

Dr Winston Abara said: "Our findings suggest that meningitis vaccines that are even only moderately effective at protecting against gonorrhoea could have a major impact on prevention and control of the disease. Clinical trials focused on the use of 4CMenB against gonorrhoea are needed to better understand its protective effects and could also offer important insights towards the development of a vaccine specifically for gonorrhoea."

Two-dose course of 4CMenB is 33% effective against gonorrhoea in adolescents and young adults

South Australia's ongoing 4CMenB vaccination programme is the most extensive globally, initially involving infants, children, adolescents, and young adults with a continuing state-funded program for infants and adolescents. In an observational study led by Professor Helen Marshall, of the Women's and Children's Hospital in Adelaide, researchers assessed the effectiveness of 4CMenB against meningitis and gonorrhoea as part of an infant, child and adolescent vaccination programme.

To estimate the effectiveness of 4CMenB against gonorrhoea, patients diagnosed with chlamydia acted as controls because of similar sexual behavioural risks reported in patients with either infection.

More than 53,000 adolescents and young adults received at least one dose of 4CMenB during the vaccination programme's first two years. As well as being highly effective against meningococcal B meningitis and sepsis, in adolescents and young adults a two-dose course of 4CMenB was 33% effective against gonorrhoea

Due to a lack of data at the time of the study, it was assumed a first vaccine dose offers no protection so only those who received a second dose were protected; however, the study by Abara and colleagues suggests one dose offers some protection, increasing the benefit of vaccination. Additionally, vaccination will reduce the future impacts of antimicrobial resistance (AMR) – which are likely to be substantial – meaning that vaccination would be even more beneficial than currently estimated, but further studies are needed to assess the potential future burden of AMR.